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Evaluation of pregnant women at risk of preterm delivery by correlating ultrasound markers with Insulin-like growth factor binding protein-1

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Abstract

The aim of the study was to assess the preterm birth risk, by correlating Actim Partus test with ultrasound markers. The present study was conducted in the Clinic of Obstetrics and Gynecology from Municipal Hospital, Craiova from Romania, on 67 pregnant women from whom we selected 34 at risk of preterm delivery with gestational ages between 22 and 32 weeks. To include pregnant women in the premature birth risk group we observed personal obstetrical history, transvaginal ultrasound cervical length (CL) (≤25 mm, ± funneling), Actim Partus test and the correlations between these elements. For inclusion in the group we need to determinate CL and test every two weeks. Our results showed that the women who had a concentration of pheripheral insulin-like growth factor binding protein-1 less than 10 ug/l (negative) did not deliver prematurely or in the next two weeks following the testing. None of the women tested gave birth before 35 weeks of pregnancy. Treatment was effective in these cases. Evidence suggests that a CL <5-25 mm increases moderately preterm birth rate at <37 weeks, although values between 20 and 25 mm do not exclude preterm birth, as well as associating funneling. Actim Partus test is a quick, facile and reliable test, which requires no additional equipment, and could be further used to monitor the rate of premature births in pregnant women.

Keywords: *pregnancy, evaluation, insulin-like growth factor*

Introduction

The preterm delivery occurs before 37 pregnancy week and the frequency is approximately between 5-15% from all deliveries. Clinical symptoms and signs are inaccurate and 50% of all pregnant women presented preterm contractions. About 20% of all symptomatic patients actually deliver preterm.

Insulin-like growth factor binding protein-1 (IGFBP-1)-Actim Partus test is the major secreted protein of human decidual cells during gestation and, as a modulator of insulin-like growth factors or by independent mechanisms, regulates embryonic implantation and growth. The protein is phosphorylated and this post-translational modification is regulated in pregnancy and represents an important determinant of its biological activity[1].

Many studies have pointed out that none of the biomarkers evaluated meet the criteria to be considered a clinically useful test to predict spontaneous preterm birth, which leads us to the idea of some associations in order to obtain valuable results[2]. Although the predictive value of the Actim Partus test is reliable, as almost all the studies until present shows can be used early in pregnancy. Taking into consideration the cost parameters that we have tried to benefit from the relation between IGFBP-1 test and the echographic examinations relating to dynamics, our study aims the preterm birth risk assessment, by correlating Actim Partus test with ultrasound markers[3,4].

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Methods

Actim Partus Test Procedure

An immunochromatographic strip test was used, based on monoclonal antibodies that detect the presence of phosphorylated IGFBP-1 protein, a binding protein in cervical secretions. Sensitivity and specificity increased Actim Partus tester and help us determine the risk of premature birth by estimating the maturation of the cervix during pregnancy. The procedure is based on the identification of increased levels of IGFBP-1 protein in the cervix as it matures.

Actim Partus tests don't require any laboratory processing. A cervical secretion sample is taken with a sterile Dacron swab from the cervix by leaving the Dacron swab in the cervix for ten to fifteen seconds. A small amount of sample could be used and can permit the swab to absorb the cervical secretion specimen. The Dacron swab is then placed in the extraction solution provided and swirled around vigorously for ten seconds. After extraction, the yellow area was inserted into the extraction solution and then keeps it until the liquid front reaches the result area.

Then, the dipstick was removed from the solution and places it in a horizontal position. A positive test result can be seen as soon as two blue lines appear in the result area. In the case of only the control line was appeared, the test result is negative. Distinct lines indicate accurate test results. Actim Partus test has been shown to be a useful predictor of preterm birth in symptomatic women. As far as we known, only few studies have conducted such research on the asimptomatic pregnant women.

Having in the view that fibronectin test is a more expensive test, we tried another possibility of prediction, this test being accessible and used in ambulatory for preterm birth risk assessment and pregnancies between 22-32 weeks.

The present prospective observational study was conducted to evaluate the efficacy of combining phIGFBP-1 and transvaginal ultrasound cervical length (CL) compared with either indicator alone in predicting pre-term labor[5].

Study group

Initial study group included 67 pregnant women, from which, respecting the criteria for inclusion remained 34 cases. Mainly, those were excluded based on the fact that they could not performed simultaneously and within the time limits measurements of cervical length and in the end without performing Actim Partus test. For 6 of the cases studied, Actim Partus test could not be performed due to contamination with outward bloody discharge through the cervix.

Results

The pregnant women in the premature birth risk group were analysed in terms of personal obstetrical history, transvaginal ultrasound CL ≤25 mm (± funneling), Actim Partus test and the correlations between these elements. Determinations of CL and test every two weeks was necessary for incursion criteria[6-9].

Of 34 pregnant women included in the survey:

- About 27 patients had a CL >3 cm and a negative Actim Partus test;
- About 3 patients with a positive Actim Partus test between 22 and 26 weeks and a CL <2.5 cm, one of these with a cervical cerclage performed in the first trimester due to personal obstetric history (Case 1) shown in Figure 1.
- One patient had a cervical cerclage at 22 weeks of pregnancy (CL=0.44 cm and funneling) (Case 2) shown in Figure 2.

From both figures, it can be observed the favorable evolution of the cases after a cerclage determined at 22 weeks of pregnancy, after the treatment. Mainly, on all the length of the pregnancy, can be observed how CL is recovering and the funneling disappears (Figures 3 and 4).

On one patient the cerclage could not be performed and the pregnancy evolved under tocolitic treatment until 36 weeks when she gave birth (Case 3, Figure 5).

The echographic evolution of CL, in time, without cerclage is illustrated in the echographic figures below. It can be observed the persistence of the funneling image and the cervical shortening (Figures 6 and 7).

For the treatment we used β-mimetics, antispasmodic, progestogens, nonsteroidal anti-inflammatory drugs and nifedipine. Further monitoring showed an increase in the CL and a negative Actim Partus test. Two of the pregnant women gave birth at over 36 weeks of pregnancy, and on one patient with positive Actim Partus test, had

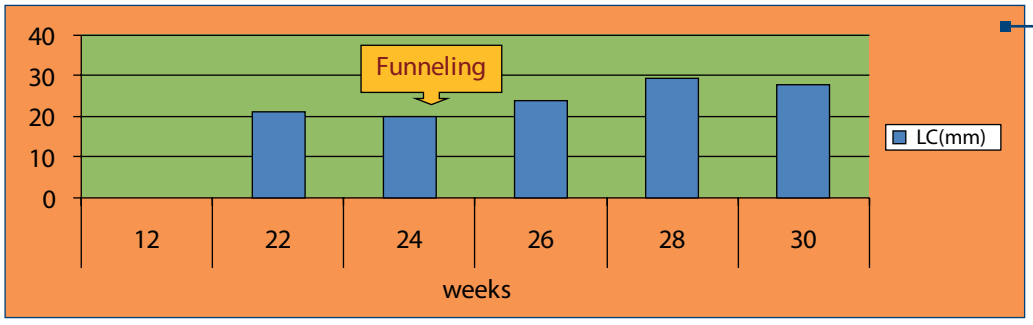

Figure 1. Case 1, evolution of cervical length in a pacient with a cervical cerclage performed in the first trimester

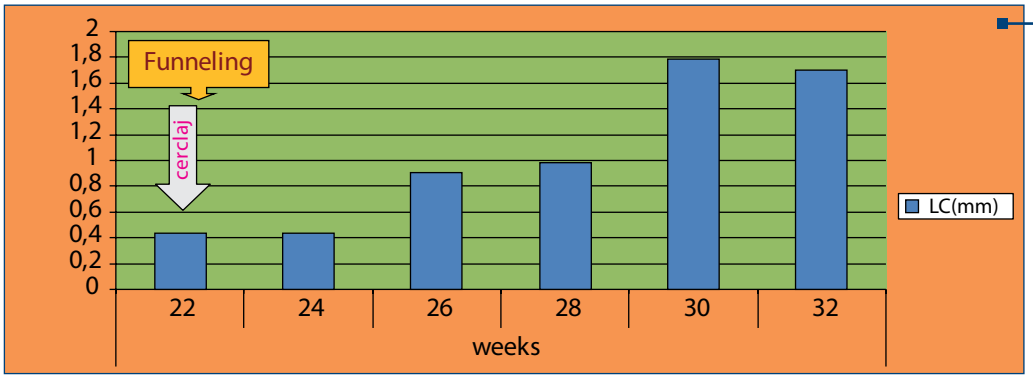

Figure 2. Case 2, evolution of cervical length in a pacient who had a cervical cerclage at 22 weeks of pregnancy

Figure 3. Cervical length 1.43 cm

Figure 4. Cervical length 0.97 cm at 28 weeks. 10 days, after cerclage at 25 weeks

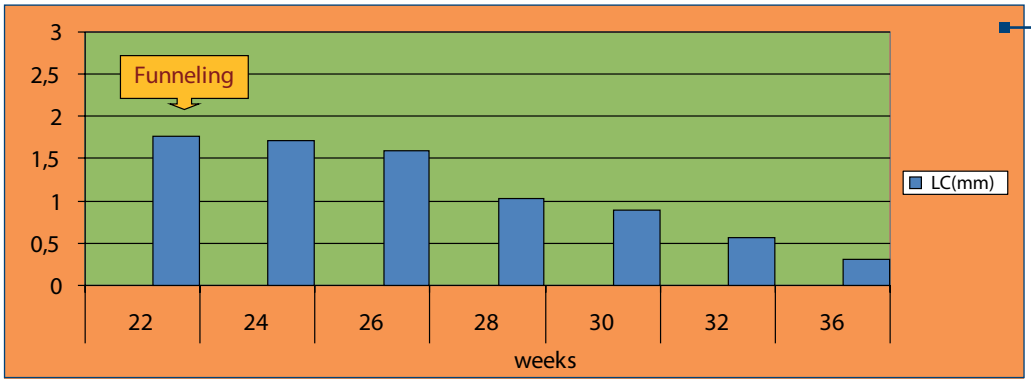

Figure 5. Case 3, evolution of cervical length in a pacient without cervical cerclage

Figure 6. Cervical length 2.17 cm at 27 weeks

Figure 7. Cervical length 1.63 cm at 30 weeks

a progressive shortening of CL, from 1.7 cm to 0.57 cm at 30 weeks, giving birth at over 36 weeks of pregnancy. A patient who underwent cerclage at 25 weeks of gestation for short cervix associated with funneling, and negative Actim Partus test, showed to develop a progressive shortening of the cervix as illustrated in Figure 8.

After a favorable evolution of both cerclage and specific treatment evolution, we observed a decrease in CL with the appearance of symptoms of preterm labor threat. At 32 weeks the patient had a CL of 0.6 cm and a satisfactory evolution under treatment. The results shows that the women who had a concentration of phGFBP - 1 less than 10 μg/l (nega-

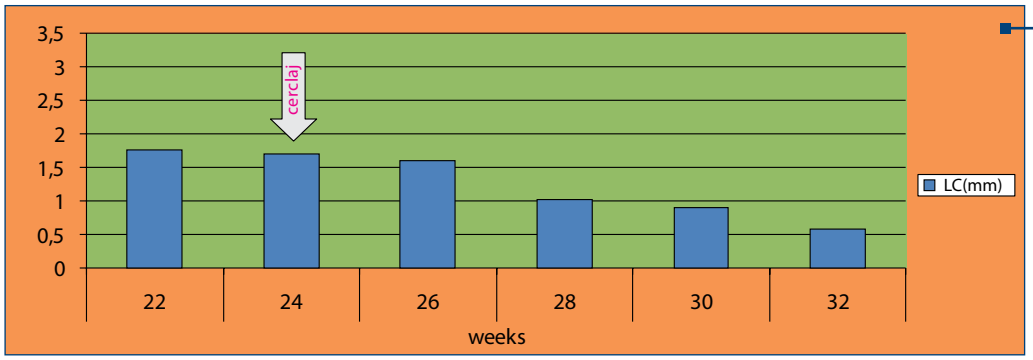

Figure 8. The evolution after cerclage. Progressive shortening of the cervix in a pacient who underwent cerclage at 25 weeks

tive) did not deliver prematurely or in the next two weeks following the testing. None of the women tested gave birth before 35 weeks of pregnancy. The treatment showed to be effective in these cases. Evidence suggests that a CL <20-25 mm increases moderately preterm birth rate <37 weeks, but values over 20 to 25 mm do not exclude preterm birth, as well as associating funneling or not.

Discussion

The higher negative predictive value of Actim Partus test indicates a safe prediction that imminent delivery is hard to achieved[10-13]. The major of patients experiencing preterm contractions will not deliver preterm and could have a negative Actim Partus test result[14]. These findings are valid for twin pregnancies with imminent preterm delivery[15]. Treating the right patients could reduce unnecessary costs and possible side-effects from medication, benefiting both the hospital and the patient. Several studies have analyzed the combinations of some predictive factors for premature delivery like the endocervical IGFBP-1 test, cervico-vaginal interleukins 6 and 8, and serum si C-reactive protein, establishing the right values for each of them[16-19]. It is known that both fetal fibronectin and IGFBP-1 tests have approximately the same ability to predict delivery under 35 weeks' gestation[18,20].

An ultrasonographic CL measurement >20 mm or a negative fetal fibronectin/IGFBP-1 test obtained from patients with uterine contractions at 24-35 weeks' gestation may avoid overdiagnosis[21,22]. Other studies presented predictive value as actim partus and analysis of CL, as well as the low gestational age when they can be considered.

Conclusions

The rapid IGFBP-1-test has a high negative predictive value for preterm delivery, associated with ultrasonographic CL measurement and we believe that monitoring these parameters can reduce the rate of premature births. By using two predictive markers of preterm birth, CL and Actim Partus test, we can considered a method for assessing changes in early pregnancy, since 22 weeks of gestation prediction of preterm birth is important in choosing therapeutic methods and clinical monitoring of pregnancy. ■

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